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Smoking during pregnancy and placental weight. A multivariate analysis on 3759 cases

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Many studies have shown that the infant's birth weight is lower when the mother smokes during pregnancy [16, 17].
The placental weight, on the other hand, appears to be only a little or not at all affected. However studies on this aspect are few and it is always difficult to prove a "non-difference." Any evalution of placental weight in relation to that of the fetus necessitates taking into account other variable factors by means of a multivariate analysis, which does not appear to have been done previously.
The present work gives the results of a prospective study carried out on 3759 cases.

1 Material and methods

From 1963 to 1969 the Institut National de la Santé et de la Recherche Médicale (I.N.S.E.R.M.) carried out a prospective study of 18,000 pregnancies in 14 Paris maternity hospitals [10]. A first analysis, carried out on a sample of 6989 women, gave the principal results on smoking [11], but the placenta was not taken into consideration.
The present work concerns a larger sample of the same population. However the total number of women is less, as the placental weight was not recorded in all the maternity hospitals from the start of the study. Women born outside France and those not giving birth in one of the hospitals participating in the study were excluded. Twins, still-births, malformed children and those cases where one of the variables considered in the multivariate analysis was missing, were also excluded, giving a total number of 3759 cases.

Curriculum vitae

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A woman smoking an average of at least one cigarette daily before the third month of pregnancy was considered to be a smoker.
The placentae were weighted with cord and membranes and the cord was cut immediately after delivery by a person who was unaware of the smoking information.

2 Results

Only 13% of the mothers smoked, 57% of them being light smokers (1—9 cigarettes per day), 26% being medium smokers (10—19 cigarettes per day) and 17% being heavy smokers (20 + cigarettes per day).
In Table I, smokers and non-smokers are compared for different characteristics; in particular, those of columns 2, 8 and 9 will be considered. The mean infant weight (IW) is lower for smokers than for non-smokers ($p < 10^{-7}$). However, the placental weight (PW) does not differ significantly, the two values being very close, and in

Tab. I. Comparison of smokers and non-smokers

	Number of cases	Birth weight (g) IW	% of weights ≦2500 g.	Height (cm)	Length of gestation (days)	% of premature birth (≦36weeks)	% small-for-date (<10 th percentile)	Weight of placenta (g) PW	PW/IW
Non-Smokers	3273	3332	3%	49.9	279.7	7%	9%	614	.185
Smokers	486	3200	9%	49.4	279.0	9%	15%	611	.193
Significance (N. S. = non-significant)		$p<10^{-7}$	$p<10^{-7}$	$p<10^{-6}$	N.S	N.S	$p<10^{-4}$	N.S	$p<10^{-6}$

consequence the PW/IW ratio is significantly higher ($p < 10^{-6}$) for smokers.

Any evaluation of a difference in placental weight in relation to a difference in fetal weight must take into account the principal factors likely to be linked to these weights, factors whose value can differ between smokers and non-smokers.

In this respect the following nine factors were considered: mother's age; her height; her usual weight; her usual blood pressures (systolic and diastolic); parity; length of gestation; sex; and family status. Regression analysis of placental weight was performed on birth weight, on smoking as well as on these 9 variables. The results (Tab. II) enable 3 categories of factors to be distinguished:

a) Infant's weight is the main factor. It is closely correlated with placental weight without taking into account other factors (r=.61), and it remains equally so (r= .59) when the other factors studied are held constant.

Tab. II. Correlation of nine variables with placental weight (PW) and with birth weight (IW), and the regression of placental weight on birth weight and these variables.

	correlation coefficient				partial correlations			
	with PW	sign.(4)	with IW	sign(4)	with PW r(1)	with PW b(2)	$t^{(3)}=b/s_b$	sign.(4)
Birth weight (g) (IW)	.61	$<10^{-9}$	—		.59	.16	44.4	$<10^{-9}$
Length of gestation (days)	.17	$<10^{-9}$	.39	$<10^{-9}$	—.10	—.69	6.2	$<10^{-9}$
Sex (♂= 1, ♀= 2)	—.05	.01	—.15	$<10^{-9}$	.07	13.3	4.3	<.001
Smoking (non-smoker=0 smoker = 1)	—.01	N.S	—.09	$<10^{-7}$	.07	18.1	4.0	<.001
Wt. of mother (Kg)	.17	$<10^{-9}$	.21	$<10^{-9}$	.05	.67	3.2	<.01
Age of mother (years)	.01	N.S	.08	$<10^{-7}$	—.04	—.84	2.6	<.05
Height of mother (cm)	.11	$<10^{-9}$	.15	$<10^{-9}$	—.01	—.18	.6	N.S
Parity	.07	$<10^{-4}$	.12	$<10^{-9}$	—.01	—.82	.6	N.S
Family status (single = 0 married = 1)	.03	N.S	.06	$<10^{-7}$	—.01	—1.34	.3	N.S
Blood pressure systolic (mm Hg)	.00	N.S	—.01	N.S	.00	—.19	.1	N.S
Blood pressure diastolic (mm Hg)	.01	N.S	.01	N.S	.01	.54	.3	N.S

(1) r = partial correlation coefficient
(2) b = partial regression coefficient
(3) t = b/s_b t test for the regression coeff. on 3757 df.
(4) N.S = non significant

b) Smoking and 4 of the 9 variables contribute individual information when the others, including birht weight, are kept constant. However, their effect is much less than that of birth weight. These "subsidiary" factors in order of decreasing importance are : 1) length of gestation, 2) sex, 3) smoking, 4) mother's weight, and 5) mother's age.
Smoking is hence one of the most important of these "subsidiary" factors. The coefficient of partial regression corresponding to smoking (18. 1) shows that in the case of a smoker, the placental weight is higher than by a non-smoker by about 18 g., assuming that birth weight and the nine other factors remain constant.

c) The 5 remaining variables are not related to placental weight when the other factors are taken into account. Their contribution is contained in the birth weight and in the above-named factors.

3 Discussion

A slightly lower placental weight among smokers was noted by O'LANE [11], TARGETT, GUNESEE, MC. BRIDE and BEISCHER [15], KULLANDER and KALLEN [7], WILSON [18], and JARVINEN and OSTERLUND [5], the amount of difference being 4, 8, 9, 11 and 13 g resprectively. However the difference is significant in only one of the studies [5]. MULCAHY, MURPHY and MARTIN [10] observed a heavier placental weight among smokers, but the difference (1 g) was not significant. An overall test (estimating the variances when these are not supplied by the authors) suggests a significantly lower placental weight among smokers, the difference being minimal.
The slightness of this difference is not due to inaccurate weighings of the placentae. This is proved by the high correlation between PW and IW ($r = .61$ in our study).
Stress was laid by WILSON in particular [6] on the higher value of PW/IW ratio among smokers resulting from the preceding facts. However this statement does not carry much weight, as an increase of this ratio is observed when IW decreases under the effect of most of the factors, and also because it does not take into account the different factors acting on PW and IW, the values of which can differ between smokers and non-smokers. It is therefore necessary to carry out a multivariate analysis which takes these factors into account. Such an analysis was made on 900 cases by ARMITAGE, BOYD, HAMILTON and ROWE [1], but the variables did not include smoking. The result was that placental weight is essentially explained by infant birth weight and two "subsidiary" factors providing complementary information: duration of gestation and the diastolic blood pressure of the mother. The present analysis gives very similar results, with closely comparable regression coefficients. In our study blood pressure has no distinct role, but it was very slight in the study of ARMITAGE, BOYD, HAMILTON and ROWE. However, 3 new factors arise, perhaps because of the greater numbers involved (the sex of the infant, the weight and age of the mother). The new result comes from taking smoking into account. **The analysis shows that smoking plays a part in determining the placental weight.** The very slight difference observed in placental weights of smokers in our survey (3 g.) results therefore, at a first approximation, from the decrease resulting solely from the lesser birth weight (132 g. $\times$ 0.16 = 21 g.) and a compensatory increase linked with smoking (18 g.). **It therefore seems clear that smoking is associated with an increase in PW when all the other factors remain constant (mainly infant's weight).**
This "**compensatory hypertrophy**" associated with hypoxia suggests a similarity with altitude effects on the one hand and anemia during pregnancy on the other hand:
In births at a high altitude the placental weight is either unchanged [9, 14], as in the case of smoking, or heavier [6] when the altitude is very high.
In severe anemia during pregnancy the placental weight is heavier, whereas the fetal weight is lower [3, 4]. However, it must be noted that a lower urinary estriol excretion has been observed in this latter case and not when the mother smokes [15].
There may well be a state of chronic hypoxia in women who smoke. It is known that a high level of carboxyhemoglobin is found in smokers and that it persists longer than was previously thought after each cigarette, resulting in chronic

hypercarboxyhemoglobinemia [8], the influence of which on the fetus, and particularly on its birth weight, has been proved [2].

However, this hypothesis does not explain why the "hypertrophic" placental weight of smokers is almost identical or even identical with that of the placental weight of non-smokers. One cannot therefore exclude the possibility that the mechanism in question is different from that mentioned above, affecting only the fetus and not the placenta (simple passive diffusion through the placental membrane for example).

Summary

The analysis of a survey of 3759 births shows that the difference in placental weight between smokers and non-smokers is, if not nil, at least minimal, and that is definitely less than might be expected taking birth weight and other factors into consideration in a multivariate analysis (Tab. II). The distortion between the fetal and placental weights, which are very closely correlated, assigns to smoking a peculiar place among the factors influencing these two weights, a result which may lead to various interpretations.

Keywords: Birth weight, placenta (weight), smoking (pregnancy).

Zusammenfassung

Nikotinabusus während der Schwangerschaft und Plazentagewicht. Eine multivariate Analyse bei 3759 Fällen

Die analytische Sichtung von 3759 Geburten zeigt, daß die Differenz zwischen dem Plazentagewicht von Raucherinnen und Nichtraucherinnen, wenn nicht null, so doch minimal ist, und sicherlich weit geringer, als zu erwarten war, wenn man das Geburtsgewicht und andere Faktoren in einer multivariaten Analyse **(Tab. II)** in die Betrachtung einbezieht. Die Verzerrung zwischen dem fetalen und plazentaren Gewicht, die eng miteinander korrelieren, weist dem Nikotingenuß eine besondere Stellung innerhalb jener Faktoren zu, welche diese beiden Gewichte beeinflussen; dieses Resultat gibt Anlaß zu den verschiedensten Interpretationen.

Schlüsselwörter: Geburtsgewicht, Plazenta (Gewicht), Rauchen (Schwangerschaft)

Résumé

Usage du tabac pendant la grossesse et poids du placenta. Analyse multivariate sur 3759 cas

L'analyse d'une enquête prospective portant sur 3759 naissances, montre que la différence du poids placentaire entre les fumeuses et les non fumeuses, est, sinon nulle, du moins minime, et certainement inférieure à celle qu'on devrait attendre en fonction du poids de naissance et d'autres facteurs pris en compte dans une analyse multivariate **(Tab. II)**. Cette distorsion entre les poids foetal et placentaire, très fortement corrélés, donne au tabagisme une place particulière parmi les facteurs influençant ces 2 poids, qui peut permettre des interprétations.

Mots-Clés: Poids de naissance, placenta (poids), tabac (grossesse).

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